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                        Utility
                        APPLICATION
                        BRINKS HOFER GILSON & LIONE, P.O. BOX 10395, CHICAGO,
                        IL, 60610
                        38
                        1
                        124 Drawing Page(s)
                        21263
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
     (FILE 'HOME' ENTERED AT 10:30:42 ON 15 JAN 2003)
     FILE 'MEDLINE, DGENE, EMBASE, SCISEARCH, USPATFULL, WPIDS, JICST-EPLUS,
     FSTA' ENTERED AT 10:31:56 ON 15 JAN 2003
           2316 S BONE MORPHOGENIC PROTEIN
          26968 S ARTICULAR CARTILAGE
            125 S OSTEOCHONDRAL GRAFT
              0 S L1 () L2 () L3
             76 S L1 AND L2
              1 S L5 AND L3
              1 S L3 AND L1
=> s 13 and regeneration
             4 L3 AND REGENERATION
=> d 18 ti abs ibib tot
     ANSWER 1 OF 4 USPATFULL
       Device for regeneration of articular cartilage and other
       An implantable device for facilitating the healing of voids in bone, `
       cartilage and soft tissue is disclosed. A preferred embodiment includes
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DOCUMENT TYPE:

FILE SEGMENT:

LEGAL REPRESENTATIVE:

NUMBER OF CLAIMS:

NUMBER OF DRAWINGS:

EXEMPLARY CLAIM:

LINE COUNT:

=> d his

L1

L2L3

L4L5

L6

L7

L8

TI

AB

a cartilage region comprising a polyelectrolytic complex joined with a subchondral bone region. The cartilage region, of this embodiment, enhances the environment for chondrocytes to grow articular cartilage; while the subchondral bone region enhances the environment for cells which migrate into that region's macrostructure and which differentiate into osteoblasts. A hydrophobic barrier exists between said regions, of this embodiment. In one embodiment, the polyelectrolytic complex transforms to hydrogel, following the implant procedure.

ACCESSION NUMBER: 2002:55324 USPATFULL

TITLE: Device for regeneration of articular

cartilage and other tissue

INVENTOR(S): Brekke, John H., Duluth, MN, UNITED STATES

Goldman, Scott M., Paoli, PA, UNITED STATES

NUMBER KIND DATE

PATENT INFORMATION: US 2002032488 A1 20020314 APPLICATION INFO.: US 2001-909027 A1 20010719 (9)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1998-206604, filed

on 7 Dec 1998, GRANTED, Pat. No. US 6264701 Division of Ser. No. US 1994-242557, filed on 13 May 1994, GRANTED,

Pat. No. US 5981825

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: Alan D. Kamrath, Kensey Nash Corporation, 55 E. Uwchlan

Avenue, Exton, PA, 19341

NUMBER OF CLAIMS: 56
EXEMPLARY CLAIM: 1
LINE COUNT: 1349

L8 ANSWER 2 OF 4 USPATFULL

TI Scaffold matrix and tissue maintaining systems

AB The invention concerns a scaffold which is used as a growth supportive base for various cells and tissue explants from three-dimensional tissue comprising naturally derived connective or skeletal tissue into attached flakes having a very high porosity. Alternatively the scaffold is

composed of fused epiphyses.

ACCESSION NUMBER: 2002:16925 USPATFULL

TITLE: Scaffold matrix and tissue maintaining systems

INVENTOR(S): Nevo, Zvi, Herzliya, ISRAEL

Robinson, Dror, Shimshon, ISRAEL

PATENT ASSIGNEE(S): RAMOT UNIVERSITY AUTHORITY FOR APPLIED RESEARCH &

INDUSTRIAL DEVELOPMENT LTD. (non-U.S. corporation)

NUMBER KIND DATE

PATENT INFORMATION: US 2002009805 A1 20020124 APPLICATION INFO.: US 2001-826389 A1 20010404 (9)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1999-345138, filed

on 6 Jul 1999, PENDING

DOCUMENT TYPE: Utility FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: LADAS & PARRY, 26 WEST 61ST STREET, NEW YORK, NY, 10023

NUMBER OF CLAIMS: 32 EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 10 Drawing Page(s)

LINE COUNT: 903

L8 ANSWER 3 OF 4 USPATFULL

TI Multi-stage collagen-based template or implant for use in the repair of

cartilage lesions

AB The invention is a template to aid in the regeneration of

articular cartilage. The template is formed by combining a porous collagen sponge ("collagen matrix") with a dense collagen membrane. The dense collagen membrane is placed on the surface of the cartilage defect to prevent cell migration from the subchondral plate and vasculature. The collagen membrane will allow movement and exchange of fluids, nutrients, cytokines and other factors necessary for cartilage regeneration. The collagen matrix has been developed to allow . attachment and growth of cells, specifically chondrocytes which are normally found in articular cartilage. The collagen matrix can be combined with chondrocytes in vitro, and therefore serve to transport cultured cells to the defect site and to retain the cells in position following implantation. Procedures are described to effectively use the two-staged template, and to fix the template to the repair site.

ACCESSION NUMBER: 2000:80202 USPATFULL

TITLE: Multi-stage collagen-based template or implant for use

in the repair of cartilage lesions

INVENTOR(S): Pachence, James M., Hopewell, NJ, United States

Frenkel, Sally, Flushing, NY, United States Menche, David, New York, NY, United States

PATENT ASSIGNEE(S): The Hospital for Joint Disease Orthopaedic Institute,

New York, NY, United States (U.S. corporation)

NUMBER KIND DATE

PATENT INFORMATION: US 6080194 20000627 APPLICATION INFO.: US 1995-385290 19950210 (8)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted

PRIMARY EXAMINER: Prebilic, Paul B.

LEGAL REPRESENTATIVE: Caesar, Rivise, Bernstein, Cohen & Pokotilow, Ltd.

NUMBER OF CLAIMS: 16 EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 4 Drawing Figure(s); 4 Drawing Page(s)

LINE COUNT: 636

- L8 ANSWER 4 OF 4 JICST-EPlus COPYRIGHT 2003 JST
- TI Four Case Reports of Mosaicplasty for Knee Joint.

 AB Repairing a defect or injury of articular cartilage is a sign
 - Repairing a defect or injury of articular cartilage is a significant challenge. Osteochondral graft, periosteal transplantation, drilling, and chondrocyte transplantation have been attempted clinically for articular surface defects. We evaluated repairs of articular cartilage by mosaicplasty. Four knees of 4 patients (2 men and 2 women) that underwent mosaicplasty were evaluated in this series. Mean patient age at surgery was 41 years. All knees underwent follow-up MRI, 2 knees underwent follow-up arthroscopy and needle biopsy after informed consent was obtained. The mean period from surgery to final follow-up was 21 months. The mean period from surgery to follow-up arthroscopy was 11 months. Four cases of mosaicplasty presented satisfactory regeneration of the articular cartilage as seem by MRI or arthroscopic examination. Two knees, after receiving mosaicplasty, demonstrated regeneration of hyaline cartilage even around the gaps in mosaicplasty, by needle biopsy. However, the structure of hyaline cartilage around the gaps in mosaicplasty differed from that of normal hyaline cartilage. Several reports described a good clinical outcome of mosaicplasty. However, only Hangody reported good hyaline cartilage regeneration at the recipient site and fibrous cartilage at the donor site. Our results demonstrated regeneration of the hyaline cartilage in the gap area of mosaicplasty, but the structure of hyaline cartilage differed from normal. There is a risk of renewed degeneration due to the poor structure of hyaline cartilage. Mosaicplasty is a sure method of repairing hyaline cartilage where there is a small defect in the articular surface. However, one report pointed out the risk of articular degeneration at the donor site after mosaicplasty. One of our cases

demonstrated bony defect at the donor site 21 months after mosaicplasty. Adequate observation of both the donor site and recipient site is needed

after mosaicplasty. (author abst.)
ACCESSION NUMBER: 1010895536 JICST-EPlus

TITLE: Four Case Reports of Mosaicplasty for Knee Joint.

AUTHOR: ICHINOHE SADAFUMI; KOYAMA AKIKO; ENDO TAKESHI; KITAGAWA

YUKA; YOSHIDA MASAAKI; SHIMAMURA TADASHI

SHIROKURA YOSHIHIRO; HONDA KEI

CORPORATE SOURCE: Iwateidai Seikeigeka

Moriokashibyoin Seikeigeka

SOURCE: Nippon Riumachi, Kansetsu Geka Gakkai Zasshi (Japanese

Journal of Rheumatism and Joint Surgery), (2001) vol. 20, no. 2, pp. 169-175. Journal Code: Y0692A (Fig. 6, Ref. 10)

ISSN: 0287-3214

PUB. COUNTRY: Japan

DOCUMENT TYPE: Journal; Short Communication

LANGUAGE: Japanese STATUS: New

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(FILE 'HOME' ENTERED AT 10:30:42 ON 15 JAN 2003)

FILE 'MEDLINE, DGENE, EMBASE, SCISEARCH, USPATFULL, WPIDS, JICST-EPLUS,

FSTA' ENTERED AT 10:31:56 ON 15 JAN 2003

L1 2316 S BONE MORPHOGENIC PROTEIN

L2 26968 S ARTICULAR CARTILAGE

L3 125 S OSTEOCHONDRAL GRAFT

L4 0 S L1 () L2 () L3

L5 76 S L1 AND L2 L6 1 S L5 AND L3

L6 1 S L5 AND L3 L7 1 S L3 AND L1

L8 4 S L3 AND REGENERATION

=> s 15 and regeneration

L9 44 L5 AND REGENERATION

=> d 19 ti abs ibib 1-15

L9 ANSWER 1 OF 44 MEDLINE

TI Cartilage and bone regeneration using gene-enhanced tissue

engineering.

AB Joint cartilage injury remains a major problem in orthopaedics with more than 500,000 cartilage repair procedures performed yearly in the United States at a cost of hundreds of millions of dollars. No consistently reliable means to regenerate joint cartilage currently exists. The

technologies of gene therapy and tissue engineering were combined using a retroviral vector to stably introduce the human bone

morphogenic protein-7 complementary deoxyribonucleic

acid into periosteal-derived rabbit mesenchymal stem cells. Bone

morphogenic protein-7 secreting gene modified cells

subsequently were expanded in monolayer culture, seeded onto polyglycolic acid grafts, implanted into a rabbit knee osteochondral defect model, and evaluated for bone and cartilage repair after 4, 8, and 12 weeks. The

grafts containing bone morphogenic protein-7

gene modified cells consistently showed complete or near complete bone and articular cartilage regeneration at 8 and 12

weeks whereas the grafts from the control groups had poor repair as judged by macroscopic, histologic, and immunohistologic criteria. This is the first report of articular cartilage

regeneration using a combined gene therapy and tissue engineering approach.

ACCESSION NUMBER: 2000488818 MEDLINE

DOCUMENT NUMBER: 20492911 PubMed ID: 11039767

TITLE: Cartilage and bone regeneration using

gene-enhanced tissue engineering.

AUTHOR: Mason J M; Breitbart A S; Barcia M; Porti D; Pergolizzi R

G; Grande D A

CORPORATE SOURCE: Department of Research, North Shore University Hospital-New

York University School of Medicine, Manhasset 11030, USA.

SOURCE: CLINICAL ORTHOPAEDICS AND RELATED RESEARCH, (2000 Oct) (379

Suppl) S171-8.

Journal code: 0075674. ISSN: 0009-921X.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals

ENTRY MONTH: 200011

ENTRY DATE: Entered STN: 20010322

Last Updated on STN: 20010322 Entered Medline: 20001103

L9 ANSWER 2 OF 44 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

TI Cartilage and bone regeneration using gene-enhanced tissue

engineering.

AB Joint cartilage injury remains a major problem in orthopaedics with more than 500,000 cartilage repair procedures performed yearly in the United States at a cost of hundreds of millions of dollars. No consistently reliable means to regenerate joint cartilage currently exists. The technologies of gene therapy and tissue engineering were combined using a retroviral vector to stably introduce the human bone

morphogenic protein-7 complementary deoxyribonucleic

acid into periosteal-derived rabbit mesenchymal stem cells. Bone

morphogenic protein-7 secreting gene modified cells

subsequently were expanded in monolayer culture, seeded onto polyglycolic acid grafts, implanted into a rabbit knee osteochondral defect model, and evaluated for bone and cartilage repair after 4, 8, and 12 weeks. The grafts containing bone morphogenic protein-7

gene modified cells consistently showed complete or near complete bone and articular cartilage regeneration at 8 and 12

weeks whereas the grafts from the control groups had poor repair as judged by macroscopic, histologic, and immunohistologic criteria. This is the first report of articular cartilage

regeneration using a combined gene therapy and tissue engineering approach.

ACCESSION NUMBER: 2000362559 EMBASE

TITLE: Cartilage and bone regeneration using

gene-enhanced tissue engineering.

AUTHOR: Mason J.M.; Breitbart A.S.; Barcia M.; Porti D.; Pergolizzi

R.G.; Grande D.A.

CORPORATE SOURCE: Dr. J.M. Mason, Gene Therapy Vector Laboratory, Department

of Research, North Shore University Hospital, 350 Community

Drive, Manhasset, NY 11030, United States

SOURCE: Clinical Orthopaedics and Related Research, (2000) -/379

SUPPL. (S171-S178).

Refs: 27

ISSN: 0009-921X CODEN: CORTBR

COUNTRY: United States

DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 022 Human Genetics
033 Orthopedic Surgery

036 Health Policy, Economics and Management

LANGUAGE: English SUMMARY LANGUAGE: English

L9 ANSWER 3 OF 44 SCISEARCH COPYRIGHT 2003 ISI (R)

TI Cartilage and bone regeneration using gene-enhanced tissue

engineering

AΒ

Joint cartilage injury remains a major problem in orthopaedics with more than 500,000 cartilage repair procedures performed yearly in the United States at a cost of hundreds of millions of dollars. No consistently reliable means to regenerate joint cartilage currently exists. The technologies of gene therapy and tissue engineering were combined using a retroviral vector to stably introduce the human hone morphogenic protein-7 complementary deoxyribonucleic acid into periosteal-derived rabbit mesenchymal stem cells. Bone

morphogenic protein-7 secreting gene modified cells subsequently were expanded in monolayer culture, seeded onto polyglycolic acid grafts, implanted into a rabbit knee osteochondral defect model, and evaluated for bone and cartilage repair after 4, 8, and 12 weeks, The grafts containing bone morphogenic protein-7

gene modified cells consistently showed complete or near complete bone and articular cartilage regeneration at 8 and 12

weeks whereas the grafts from the control groups had poor repair as judged by macroscopic, histologic, and immunohistologic criteria, This is the first report of articular cartilage

regeneration using a combined gene therapy and tissue engineering approach.

ACCESSION NUMBER: 2000:777821 SCISEARCH

THE GENUINE ARTICLE: 362NP

TITLE: Cartilage and bone regeneration using

gene-enhanced tissue engineering

AUTHOR: Mason J M (Reprint); Breitbart A S; Barcia M; Porti D;

Pergolizzi R G; Grande D A

CORPORATE SOURCE: NYU, GENE THERAPY VECTOR LAB, DEPT RES, N SHORE UNIV HOSP,

SCH MED, 350 COMMUNITY DR, MANHASSET, NY 11030 (Reprint); NYU, DIV PLAST & RECONSTRUCT SURG, SCH MED, N SHORE UNIV HOSP, MANHASSET, NY 11030; NYU, DIV ORTHOPED SURG, SCH MED, N SHORE UNIV HOSP, DEPT SURG, MANHASSET, NY 11030

COUNTRY OF AUTHOR:

SOURCE:

DOCUMENT TYPE:

CLINICAL ORTHOPAEDICS AND RELATED RESEARCH, (OCT 2000) No.

379, Supp. [S], pp. S171-S178.

Publisher: LIPPINCOTT WILLIAMS & WILKINS, 530 WALNUT ST,

PHILADELPHIA, PA 19106-3621.

ISSN: 0009-921X. Article; Journal

FILE SEGMENT: LIFE; CLIN

LANGUAGE: English REFERENCE COUNT: 27

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L9 ANSWER 4 OF 44 USPATFULL

TI Secreted and transmembrane polypeptides and nucleic acids encoding the same

The present invention is directed to novel polypeptides and to nucleic acid molecules encoding those polypeptides. Also provided herein are vectors and host cells comprising those nucleic acid sequences, chimeric polypeptide molecules comprising the polypeptides of the present invention fused to heterologous polypeptide sequences, antibodies which bind to the polypeptides of the present invention and to methods for producing the polypeptides of the present invention.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 2003:3495 USPATFULL

TITLE: Secreted and transmembrane polypeptides and nucleic

acids encoding the same

INVENTOR(S): Ashkenazi, Avi, San Mateo, CA, UNITED STATES

Botstein, David, Belmont, CA, UNITED STATES Desnoyers, Luc, San Francisco, CA, UNITED STATES Eaton, Dan L., San Rafael, CA, UNITED STATES

Ferrara, Napoleone, San Francisco, CA, UNITED STATES

Filvaroff, Ellen, San Francisco, CA, UNITED STATES Fong, Sherman, Alameda, CA, UNITED STATES Gao, Wei-Qiang, Palo Alto, CA, UNITED STATES Gerber, Hanspeter, San Francisco, CA, UNITED STATES Gerritsen, Mary E., San Mateo, CA, UNITED STATES Goddard, Audrey, San Francisco, CA, UNITED STATES Godowski, Paul J., Burlingame, CA, UNITED STATES Grimaldi, J. Christopher, San Francisco, CA, UNITED STATES

Gurney, Austin L., Belmont, CA, UNITED STATES Hillan, Kenneth J., San Francisco, CA, UNITED STATES Kljavin, Ivar J., Lafayette, CA, UNITED STATES Mather, Jennie P., Millbrae, CA, UNITED STATES Pan, James, Belmont, CA, UNITED STATES Paoni, Nicholas F., Belmont, CA, UNITED STATES Roy, Margaret Ann, San Francisco, CA, UNITED STATES Stewart, Timothy A., San Francisco, CA, UNITED STATES Tumas, Daniel, Orinda, CA, UNITED STATES Williams, P. Mickey, Half Moon Bay, CA, UNITED STATES Wood, William I., Hillsborough, CA, UNITED STATES Genentech, Inc. (U.S. corporation)

PATENT ASSIGNEE(S):

NUMBER KIND DATE -----

PATENT INFORMATION: APPLICATION INFO .:

US 2003003530 A1 20030102 US 2001-904011 A1 20010711 (9)

RELATED APPLN. INFO.:

Continuation of Ser. No. US 2000-665350, filed on 18

DATE

Sep 2000, PENDING

NUMBER

PRIORITY INFORMATION:

WO	1998-US18824	19980910	
WO	1998-US19177	19980914	
	1998-US19330		
	1998-US19437		
	1998-US25108	19981201	
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DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: BRINKS HOFER GILSON & LIONE, P.O. BOX 10395, CHICAGO,

IL, 60610

NUMBER OF CLAIMS: 38 EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 124 Drawing Page(s)

LINE COUNT: 21255

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 5 OF 44 USPATFULL

TI Secreted and transmembrane polypeptides and nucleic acids encoding the same

The present invention is directed to novel polypeptides and to nucleic acid molecules encoding those polypeptides. Also provided herein are vectors and host cells comprising those nucleic acid sequences, chimeric polypeptide molecules comprising the polypeptides of the present invention fused to heterologous polypeptide sequences, antibodies which bind to the polypeptides of the present invention and to methods for

producing the polypeptides of the present invention.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 2002:344632 USPATFULL

Secreted and transmembrane polypeptides and nucleic TITLE:

acids encoding the same

Ashkenazi, Avi, San Mateo, CA, UNITED STATES INVENTOR (S):

Botstein, David, Belmont, CA, UNITED STATES Desnoyers, Luc, San Francisco, CA, UNITED STATES

Eaton, Dan L., San Rafael, CA, UNITED STATES

Ferrara, Napoleone, San Francisco, CA, UNITED STATES Filvaroff, Ellen, San Francisco, CA, UNITED STATES

Fong, Sherman, Alameda, CA, UNITED STATES

Gao, Wei-Qiang, Palo Alto, CA, UNITED STATES

Gerber, Hanspeter, San Francisco, CA, UNITED STATES Gerritsen, Mary E., San Mateo, CA, UNITED STATES Goddard, Audrey, San Francisco, CA, UNITED STATES Godowski, Paul J., Burlingame, CA, UNITED STATES Grimaldi, J. Christopher, San Francisco, CA, UNITED

STATES

Gurney, Austin L., Belmont, CA, UNITED STATES

Hillan, Kenneth J., San Francisco, CA, UNITED STATES

Kljavin, Ivar J., Lafayette, CA, UNITED STATES Mather, Jennie P., Millbrae, CA, UNITED STATES

Pan, James, Belmont, CA, UNITED STATES

Paoni, Nicholas F., Belmont, CA, UNITED STATES Roy, Margaret Ann, San Francisco, CA, UNITED STATES Stewart, Timothy A., San Francisco, CA, UNITED STATES

Tumas, Daniel, Orinda, CA, UNITED STATES

Williams, P. Mickey, Half Moon Bay, CA, UNITED STATES

Wood, William I., Hillsborough, CA, UNITED STATES

PATENT ASSIGNEE(S): Genentech, Inc. (U.S. corporation)

NUMBER KIND DATE ______

PATENT INFORMATION: APPLICATION INFO.:

US 2002198366 A1 20021226 US 2001-907841 A1 20010717 (9)

RELATED APPLN. INFO.:

Continuation of Ser. No. US 2000-665350, filed on 18

Sep 2000, PENDING

NUMBER

PRIORITY INFORMATION:

WO 1998-US18824 19980910 WO 1998-US19177 19980914 WO 1998-US19330 19980916 WO 1998-US19437 19980917 WO 1998-US25108 19981201 WO 1999-US20594 19990908 WO 1999-US20944 19990913 WO 1999-US21090 19990915 WO 1999-US21547 19990915 WO 1999-US23089 19991005 WO 1999-US28214 19991129 WO 1999-US28313 19991130 WO 1999-US28301 19991201 WO 1999-US28564 19991202 WO 1999-US28565 19991202 WO 1999-US30095 19991216 WO 1999-US30999 19991220 WO 1999-US30911 19991220 WO 2000-US219 20000105 WO 2000-US3565 WO 2000-US3565 WO 2000-US4414 WO 2000-US5004 20000211 20000222 20000224

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US 1997-66453P
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Utility
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DOCUMENT TYPE:
FILE SEGMENT:
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LEGAL REPRESENTATIVE: BRINKS HOFER GILSON & LIONE, P.O. BOX 10395, CHICAGO,

IL, 60610

APPLICATION

NUMBER OF CLAIMS: 38 EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 124 Drawing Page(s)

LINE COUNT: 21263

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ANSWER 6 OF 44 USPATFULL T.9

Secreted and transmembrane polypeptides and nucleic acids encoding the ΤI

The present invention is directed to novel polypeptides and to nucleic AB acid molecules encoding those polypeptides. Also provided herein are vectors and host cells comprising those nucleic acid sequences, chimeric polypeptide molecules comprising the polypeptides of the present invention fused to heterologous polypeptide sequences, antibodies which bind to the polypeptides of the present invention and to methods for producing the polypeptides of the present invention.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:

2002:343945 USPATFULL

TITLE:

Secreted and transmembrane polypeptides and nucleic

acids encoding the same

INVENTOR(S):

Ashkenazi, Avi, San Mateo, CA, UNITED STATES Botstein, David, Belmont, CA, UNITED STATES Desnoyers, Luc, San Francisco, CA, UNITED STATES Eaton, Dan L., San Rafael, CA, UNITED STATES Ferrara, Napoleone, San Francisco, CA, UNITED STATES Filvaroff, Ellen, San Francisco, CA, UNITED STATES Fong, Sherman, Alameda, CA, UNITED STATES Gao, Wei-Qiang, Palo Alto, CA, UNITED STATES

Gerber, Hanspeter, San Francisco, CA, UNITED STATES Gerritsen, Mary E., San Mateo, CA, UNITED STATES Goddard, Audrey, San Francisco, CA, UNITED STATES Godowski, Paul J., Burlingame, CA, UNITED STATES Grimaldi, J. Christopher, San Francisco, CA, UNITED

STATES

Gurney, Austin L., Belmont, CA, UNITED STATES Hillan, Kenneth J., San Francisco, CA, UNITED STATES Kljavin, Ivar J., Lafayette, CA, UNITED STATES Mather, Jennie P., Millbrae, CA, UNITED STATES Pan, James, Belmont, CA, UNITED STATES

Paoni, Nicholas F., Belmont, CA, UNITED STATES Roy, Margaret Ann, San Francisco, CA, UNITED STATES Stewart, Timothy A., San Francisco, CA, UNITED STATES

Tumas, Daniel, Orinda, CA, UNITED STATES

Williams, P. Mickey, Half Moon Bay, CA, UNITED STATES Wood, William I., Hillsborough, CA, UNITED STATES

PATENT ASSIGNEE(S): Genentech, Inc. (U.S. corporation)

> NUMBER KIND DATE US 2002197671 A1 20021226 US 2001-907824 A1 20010717

PATENT INFORMATION: APPLICATION INFO.: RELATED APPLN. INFO.:

20010717 (9) Continuation of Ser. No. US 2000-665350, filed on 18

19991005

19991129

Sep 2000, PENDING

WO 1999-US23089

WO 1999-US28214

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US 1997-66770P 19971124 (60) US 1997-66511P 19971124 (60) US 1997-66453P 19971124 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: BRINKS HOFER GILSON & LIONE, P.O. BOX 10395, CHICAGO,

IL, 60610

NUMBER OF CLAIMS: 38 EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 124 Drawing Page(s)

LINE COUNT: 22162

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 7 OF 44 USPATFULL

TI Methods of using bone morphogenic proteins as biomarkers for determining

cartilage degeneration and aging

Methods are provided for determining cartilage degeneration, regeneration, or aging in a joint tissue in a patient by measuring levels of osteogenic protein-1 (OP-1) protein and/or mRNA in synovial fluid or joint tissue. The methods according to the invention are useful for detecting, diagnosing, predicting, determining a

predisposition for, or monitoring joint tissue degeneration, regeneration, or aging in a patient including inflammatory joint

disease or age-related disorders.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 2002:337321 USPATFULL

TITLE: Methods of using bone morphogenic proteins as

biomarkers for determining cartilage degeneration and

aging

INVENTOR(S): Chubinskaya, Susanna, Vernon Hills, IL, UNITED STATES

Rueger, David C., Southborough, MA, UNITED STATES Kuettner, Klaus E., Chicago, IL, UNITED STATES

APPLICATION INFO.: US 2002-81163 A1 20020220 (10)

NUMBER DATE

PRIORITY INFORMATION: US 2001-348111P 20011109 (60)
US 2001-270528P 20010221 (60)

DOCUMENT TYPE: Utility FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: TESTA, HURWITZ & THIBEAULT, LLP, HIGH STREET TOWER, 125

HIGH STREET, BOSTON, MA, 02110

NUMBER OF CLAIMS: 47 EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 15 Drawing Page(s)

LINE COUNT: 1482

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 8 OF 44 USPATFULL

TI Secreted and transmembrane polypeptides and nucleic acids encoding the same

The present invention is directed to novel polypeptides and to nucleic acid molecules encoding those polypeptides. Also provided herein are vectors and host cells comprising those nucleic acid sequences, chimeric polypeptide molecules comprising the polypeptides of the present invention fused to heterologous polypeptide sequences, antibodies which bind to the polypeptides of the present invention and to methods for producing the polypeptides of the present invention.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

2002:337301 USPATFULL ACCESSION NUMBER:

Secreted and transmembrane polypeptides and nucleic TITLE:

acids encoding the same

Ashkenazi, Avi, San Mateo, CA, UNITED STATES INVENTOR (S):

Botstein, David, Belmont, CA, UNITED STATES Desnoyers, Luc, San Francisco, CA, UNITED STATES Eaton, Dan L., San Rafael, CA, UNITED STATES

Ferrara, Napoleone, San Francisco, CA, UNITED STATES Filvaroff, Ellen, San Francisco, CA, UNITED STATES

Fong, Sherman, Alameda, CA, UNITED STATES

Gao, Wei-Qiang, Palo Alto, CA, UNITED STATES

Gerber, Hanspeter, San Francisco, CA, UNITED STATES Gerritsen, Mary E., San Mateo, CA, UNITED STATES Goddard, Audrey, San Francisco, CA, UNITED STATES Godowski, Paul J., Burlingame, CA, UNITED STATES Grimaldi, J. Christopher, San Francisco, CA, UNITED

STATES

Gurney, Austin L., Belmont, CA, UNITED STATES

Hillan, Kenneth J., San Francisco, CA, UNITED STATES Kljavin, Ivar J., Lafayette, CA, UNITED STATES

Mather, Jennie P., Millbrae, CA, UNITED STATES Pan, James, Belmont, CA, UNITED STATES

Paoni, Nicholas F., Belmont, CA, UNITED STATES Roy, Margaret Ann, San Francisco, CA, UNITED STATES Stewart, Timothy A., San Francisco, CA, UNITED STATES

Tumas, Daniel, Orinda, CA, UNITED STATES

Williams, P. Mickey, Half Moon Bay, CA, UNITED STATES

Wood, Wlliam I., Hillsborough, CA, UNITED STATES

Genentech, Inc. (U.S. corporation) PATENT ASSIGNEE(S):

> KIND NUMBER DATE -----

PATENT INFORMATION: APPLICATION INFO.:

US 2002192659 A1 20021219 US 2001-902853 A1 20010710

RELATED APPLN. INFO.:

Continuation of Ser. No. US 2000-665350, filed on 18

Sep 2000, PENDING

NUMBER DATE PRIORITY INFORMATION: WO 1998-US18824 19980910 WO 1998-US19177 19980914 WO 1998-US19330 19980916 WO 1998-US19437 19980917

> WO 1998-US25108 19981201 WO 1999-US20594 19990908 WO 1999-US20944 19990913 WO 1999-US21090 19990915 WO 1999-US21547 19990915

WO 1999-US23089 19991005 WO 1999-US28214 19991129

WO 1999-US28313 19991130 WO 1999-US28301 19991201

WO 1999-US28564 19991202 WO 1999-US28565 19991202

WO 1999-US30095 19991216 WO 1999-US30999 19991220

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WO 2000-US5004 20000224

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                        Utility
                        APPLICATION
                        BRINKS HOFER GILSON & LIONE, P.O. BOX 10395, CHICAGO,
                         IL, 60610
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                         124 Drawing Page(s)
                         21726
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
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DOCUMENT TYPE:

FILE SEGMENT:

LINE COUNT:

NUMBER OF CLAIMS:

EXEMPLARY CLAIM:

NUMBER OF DRAWINGS:

LEGAL REPRESENTATIVE:

L9 ANSWER 9 OF 44 USPATFULL

TI Peptide scaffold encapsulation of tissue cells and uses thereof

AB The invention features peptide scaffolds that are useful in the repair and replacement of various tissues. The invention also provides methods for making these scaffolds and methods for using them.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 2002:287608 USPATFULL

TITLE: Peptide scaffold encapsulation of tissue cells and uses

thereof

INVENTOR(S): Kisiday, John, Watertown, MA, UNITED STATES

Grodzinsky, Alan, Lexington, MA, UNITED STATES Zhang, Shuguang, Lexington, MA, UNITED STATES

NUMBER KIND DATE
-----US 2002160471 A1 20021031

PATENT INFORMATION: US 2002160471 A1 20021031 APPLICATION INFO.: US 2001-778200 A1 20010206 (9)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: CLARK & ELBING LLP, 101 FEDERAL STREET, BOSTON, MA,

02110

NUMBER OF CLAIMS: 18 EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 9 Drawing Page(s)

LINE COUNT: 1010

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 10 OF 44 USPATFULL

TI Secreted and transmembrane polypeptides and nucleic acids encoding the

The present invention is directed to novel polypeptides and to nucleic acid molecules encoding those polypeptides. Also provided herein are vectors and host cells comprising those nucleic acid sequences, chimeric polypeptide molecules comprising the polypeptides of the present invention fused to heterologous polypeptide sequences, antibodies which bind to the polypeptides of the present invention and to methods for producing the polypeptides of the present invention.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 2002:287511 USPATFULL

TITLE: Secreted and transmembrane polypeptides and nucleic

acids encoding the same

INVENTOR(S): Ashkenazi, Avi, San Mateo, CA, UNITED STATES

Botstein, David, Belmont, CA, UNITED STATES
Desnoyers, Luc, San Francisco, CA, UNITED STATES
Eaton, Dan L., San Rafael, CA, UNITED STATES

Ferrara, Napoleone, San Francisco, CA, UNITED STATES Filvaroff, Ellen, San Francisco, CA, UNITED STATES

Fong, Sherman, Alameda, CA, UNITED STATES
Gao, Wei-Qiang, Palo Alto, CA, UNITED STATES

Gerber, Hanspeter, San Francisco, CA, UNITED STATES Gerritsen, Mary E., San Mateo, CA, UNITED STATES Goddard, Audrey, San Francisco, CA, UNITED STATES Godowski, Paul J., Burlingame, CA, UNITED STATES Grimaldi, J. Christopher, San Francisco, CA, UNITED

STATES

Gurney, Austin L., Belmont, CA, UNITED STATES Hillan, Kenneth J., San Francisco, CA, UNITED STATES Kljavin, Ivar J., Lafayette, CA, UNITED STATES Mather, Jennie P., Millbrae, CA, UNITED STATES

Pan, James, Belmont, CA, UNITED STATES

Paoni, Nicholas F., Belmont, CA, UNITED STATES Roy, Margaret Ann, San Francisco, CA, UNITED STATES Stewart, Timothy A., San Francisco, CA, UNITED STATES Tumas, Daniel, Orinda, CA, UNITED STATES Williams, P. Mickey, Half Moon Bay, CA, UNITED STATES Wood, William I., Hillsborough, CA, UNITED STATES

DATE

PATENT ASSIGNEE(S): Genentech, Inc. (U.S. corporation)

RELATED APPLN. INFO.: Continuation of Ser. No. US 2000-665350, filed on 18

NUMBER

Sep 2000, PENDING

PRIORITY INFORMATION:

WO	1998-US18824	19980910	
WO		19980914	
WO	1998-US19330	19980916	
WO	1998-US19437	19980917	
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WO	1999-US20594		
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US 1997-66453P
Utility
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DOCUMENT TYPE:

FILE SEGMENT:

APPLICATION

LEGAL REPRESENTATIVE:

BRINKS HOFER GILSON & LIONE, P.O. BOX 10395, CHICAGO,

IL, 60610

NUMBER OF CLAIMS:

EXEMPLARY CLAIM:

NUMBER OF DRAWINGS:

124 Drawing Page(s)

LINE COUNT:

21310

38

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ANSWER 11 OF 44 USPATFULL L9

Secreted and transmembrane polypeptides and nucleic acids encoding the TI

The present invention is directed to novel polypeptides and to nucleic AΒ acid molecules encoding those polypeptides. Also provided herein are vectors and host cells comprising those nucleic acid sequences, chimeric polypeptide molecules comprising the polypeptides of the present invention fused to heterologous polypeptide sequences, antibodies which bind to the polypeptides of the present invention and to methods for producing the polypeptides of the present invention.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:

2002:265833 USPATFULL

TITLE:

Secreted and transmembrane polypeptides and nucleic

acids encoding the same

INVENTOR(S):

Ashkenazi, Avi, San Mateo, CA, UNITED STATES Botstein, David, Belmont, CA, UNITED STATES Desnoyers, Luc, San Francisco, CA, UNITED STATES Eaton, Dan L., San Rafael, CA, UNITED STATES Ferrara, Napoleone, San Francisco, CA, UNITED STATES Filvaroff, Ellen, San Francisco, CA, UNITED STATES Fong, Sherman, Alameda, CA, UNITED STATES Gao, Wei-Qiang, Palo Alto, CA, UNITED STATES Gerber, Hanspeter, San Francisco, CA, UNITED STATES Gerritsen, Mary E., San Mateo, CA, UNITED STATES

Goddard, Audrey, San Francisco, CA, UNITED STATES Godowski, Paul J., Burlingame, CA, UNITED STATES Grimaldi, J. Christopher, San Francisco, CA, UNITED STATES

Gurney, Austin L., Belmont, CA, UNITED STATES Hillan, Kenneth J., San Francisco, CA, UNITED STATES Kljavin, Ivar J., Lafayette, CA, UNITED STATES Mather, Jennie P., Millbrae, CA, UNITED STATES Pan, James, Belmont, CA, UNITED STATES

Paoni, Nicholas F., Belmont, CA, UNITED STATES Roy, Margaret Ann, San Francisco, CA, UNITED STATES Stewart, Timothy A., San Francisco, CA, UNITED STATES Tumas, Daniel, Orinda, CA, UNITED STATES

Williams, P. Mickey, Half Moon Bay, CA, UNITED STATES Wood, William I., Hillsborough, CA, UNITED STATES Genentech, Inc. (U.S. corporation)

PATENT ASSIGNEE(S):

KIND DATE NUMBER

PATENT INFORMATION: APPLICATION INFO.: RELATED APPLN. INFO.:

_____ US 2002146709 A1 20021010 US 2001-909088 A1 20010718 (9)

Continuation of Ser. No. US 2000-665350, filed on 18

DATE

Sep 2000, PENDING

NUMBER

PRIORITY INFORMATION:

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WO	1998-US19177		
WO	1998-US19330	19980916	
WO	1998-US19437	19980917	
WO	1998-US25108	19981201	
WO	1999-US20594	19990908	
WO	1999-US20944	19990913	
MO	1999-US21090	19990915 19990915	
WO	1999-US21547		
WO WO	1999-US23089 1999-US28214	19991005 19991129	
WO	1999-US28214 1999-US28313	19991129	
WO	1999-US28301	19991201	
WO	1999-US28564	19991201	
WO	1999-US28565	19991202	
WO	1999-US30095	19991216	
WO	1999-US30999	19991220	
WO	1999-US30911	19991220	
WO	2000-US219	20000105	
WO	2000 US215	20000211	
WO	2000-US4414	20000222	
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US 1997-66511P
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US 1997-66453P
                   19971124 (60)
Utility
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DOCUMENT TYPE:

APPLICATION

FILE SEGMENT: LEGAL REPRESENTATIVE:

BRINKS HOFER GILSON & LIONE, P.O. BOX 10395, CHICAGO,

IL, 60610

38

NUMBER OF CLAIMS: EXEMPLARY CLAIM:

NUMBER OF DRAWINGS: 124 Drawing Page(s)

LINE COUNT: 21668

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

- L9 ANSWER 12 OF 44 USPATFULL
- TI Bone morphogenic protein (BMP)

polynucleotides, polypeptides, and antibodies

The present invention relates to novel human BMP polypeptides and isolated nucleic acids containing the coding regions of the genes encoding such polypeptides. Also provided are vectors, host cells, antibodies, and recombinant methods for producing human BMP polypeptides. The invention further relates to diagnostic and therapeutic methods useful for diagnosing and treating disorders related to these novel human BMP polypeptides.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 2002:259593 USPATFULL

TITLE: Bone morphogenic protein

(BMP) polynucleotides, polypeptides, and antibodies

Ni, Jian, Germantown, MD, UNITED STATES Ruben, Steven M., Olney, MD, UNITED STATES Shi, Yanggu, Gaithersburg, MD, UNITED STATES

Human Genome Sciences, Inc., Rockville, MD, UNITED

PATENT ASSIGNEE(S):

STATES, 20850 (U.S. corporation)

KIND DATE NUMBER _____ US 2002143170 A1 20021003 US 2002-67422 A1 20020207 (10) PATENT INFORMATION:

APPLICATION INFO.:

Continuation of Ser. No. US 2000-685899, filed on 11 RELATED APPLN. INFO.: Oct 2000, PENDING Continuation-in-part of Ser. No. WO

2000-US9028, filed on 6 Apr 2000, UNKNOWN

NUMBER DATE**....** US 1999-130693P 19990423 (60) PRIORITY INFORMATION: US 1999-131672P 19990429 (60) US 1999-147020P 19990803 (60) US 1999-152933P 19990909 (60)

DOCUMENT TYPE: Utility FILE SEGMENT: APPLICATION

HUMAN GENOME SCIENCES INC, 9410 KEY WEST AVENUE, LEGAL REPRESENTATIVE:

ROCKVILLE, MD, 20850

22 NUMBER OF CLAIMS: EXEMPLARY CLAIM: LINE COUNT: 10845

INVENTOR(S):

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ANSWER 13 OF 44 USPATFULL

Secreted and transmembrane polypeptides and nucleic acids encoding the ΤI

The present invention is directed to novel polypeptides and to nucleic AB acid molecules encoding those polypeptides. Also provided herein are vectors and host cells comprising those nucleic acid sequences, chimeric polypeptide molecules comprising the polypeptides of the present invention fused to heterologous polypeptide sequences, antibodies which bind to the polypeptides of the present invention and to methods for producing the polypeptides of the present invention.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

2002:243054 USPATFULL ACCESSION NUMBER:

Secreted and transmembrane polypeptides and nucleic TITLE:

acids encoding the same

Ashkenazi, Avi, San Mateo, CA, UNITED STATES INVENTOR(S):

Botstein, David, Belmont, CA, UNITED STATES Desnoyers, Luc, San Francisco, CA, UNITED STATES Eaton, Dan L., San Rafael, CA, UNITED STATES

Ferrara, Napoleone, San Francisco, CA, UNITED STATES Filvaroff, Ellen, San Francisco, CA, UNITED STATES

Fong, Sherman, Alameda, CA, UNITED STATES Gao, Wei-Qiang, Palo Alto, CA, UNITED STATES

Gerber, Hanspeter, San Francisco, CA, UNITED STATES Gerritsen, Mary E., San Mateo, CA, UNITED STATES Goddard, Audrey, San Francisco, CA, UNITED STATES Godowski, Paul J., Burlingame, CA, UNITED STATES Grimaldi, J. Christopher, San Francisco, CA, UNITED

STATES

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Williams, P. Mickey, Half Moon Bay, CA, UNITED STATES
Wood, William I., Hillsborough, CA, UNITED STATES
Genentech, Inc. (U.S. corporation)

PATENT ASSIGNEE(S):

NUMBER KIND DATE
----US 2002132240 A1 20020919
US 2001-909320 A1 20010718 (9)

PATENT INFORMATION: APPLICATION INFO.: RELATED APPLN. INFO.:

US 2001-909320 Al 20010718 (9) Continuation of Ser. No. US 2000-665350, filed on 18

DATE

Sep 2000, PENDING

NUMBER

PRIORITY INFORMATION:

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WO	1998-US18824	19980910	
WO	1998-US19177	19980914	
WO	1998-US19330	19980916	
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WO	1998-US25108	19981201	
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US 1997-66453P
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DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: BRINKS HOFER GILSON & LIONE, P.O. BOX 10395, CHICAGO,

IL, 60610

NUMBER OF CLAIMS: 38 EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 124 Drawing Page(s)

LINE COUNT: 21778

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 14 OF 44 USPATFULL

TI Use of adipose tissue-derived stromal cells for chondrocyte differentiation and cartilage repair

Methods and compositions for directing adipose-derived stromal cells cultivated in vitro to differentiate into cells of the chondrocyte lineage are disclosed. The invention further provides a variety of chondroinductive agents which can be used singly or in combination with other nutrient components to induce chondrogenesis in adipose-derived stromal cells either in cultivating monolayers or in a biocompatible lattice or matrix in a three-dimensional configuration. Use of the differentiated chondrocytes for the therapeutic treatment of a number of human conditions and diseases including repair of cartilage in vivo is disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 2002:214259 USPATFULL

TITLE: Use of adipose tissue-derived stromal cells for chondrocyte differentiation and cartilage repair

choldrocyte differentiation and cartinage repair

INVENTOR(S): Halvorsen, Yuan-Di C., Holly Springs, NC, UNITED STATES Wilkison, William O., Bahama, NC, UNITED STATES

Gimble, Jeffrey Martin, Chapel Hill, NC, UNITED STATES

NUMBER KIND DATE

PATENT INFORMATION: US 2002115647 A1 20020822 APPLICATION INFO.: US 2002-125106 A1 20020418 (10)

APPLICATION INFO.:

Continuation of Ser. No. US 2000-573989, filed on 17 RELATED APPLN. INFO.:

May 2000, PENDING

NUMBER DATE

______ US 1999-149850P 19990819 (60) PRIORITY INFORMATION:

DOCUMENT TYPE: Utility APPLICATION FILE SEGMENT:

KING & SPALDING, 191 PEACHTREE STREET, N.E., ATLANTA, LEGAL REPRESENTATIVE:

GA, 30303-1763

NUMBER OF CLAIMS: 18 EXEMPLARY CLAIM:

NUMBER OF DRAWINGS: 5 Drawing Page(s)

831 LINE COUNT:

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ANSWER 15 OF 44 USPATFULL

Use of adipose tissue-derived stromal cells for chondrocyte ΤI

differentiation and cartilage repair

AB Methods and compositions for directing adipose-derived stromal cells cultivated in vitro to differentiate into cells of the chondrocyte lineage are disclosed. The invention further provides a variety of chondroinductive agents which can be used singly or in combination with other nutrient components to induce chondrogenesis in adipose-derived stromal cells either in cultivating monolayers or in a biocompatible lattice or matrix in a three-dimensional configuration. Use of the differentiated chondrocytes for the therapeutic treatment of a number of human conditions and diseases including repair of cartilage in vivo is disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 2002:194742 USPATFULL

Use of adipose tissue-derived stromal cells for TITLE:

chondrocyte differentiation and cartilage repair

Halvorsen, Yuan-Di C., Holly Springs, NC, United States INVENTOR(S):

Wilkison, William O., Bahama, NC, United States

Gimble, Jeffrey Martin, Chapel Hill, NC, United States

Artecel Science, Inc., Durham, NC, United States (U.S. PATENT ASSIGNEE(S):

corporation)

NUMBER KIND DATE

PATENT INFORMATION: US 6429013 B1 20020806 US 2000-573989 20000517 20000517 (9) APPLICATION INFO.:

> NUMBER DATE ______

PRIORITY INFORMATION: US 1999-149850P 19990819 (60)

DOCUMENT TYPE: Utility GRANTED FILE SEGMENT: Guzo, David PRIMARY EXAMINER:

Davis, Katharine F ASSISTANT EXAMINER:

LEGAL REPRESENTATIVE: King & Spalding, Knowles, Sherry M., Bennett-Paris,

Joseph

NUMBER OF CLAIMS: EXEMPLARY CLAIM:

5 Drawing Figure(s); 5 Drawing Page(s) NUMBER OF DRAWINGS:

LINE COUNT: 995

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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LOGINID:ssspta1653hxp PASSWORD: TERMINAL (ENTER 1, 2, 3, OR ?):2 Welcome to STN International Web Page URLs for STN Seminar Schedule - N. America "Ask CAS" for self-help around the clock NEWS Apr 08 BEILSTEIN: Reload and Implementation of a New Subject Area NEWS Apr 09 ZDB will be removed from STN NEWS Apr 09 US Patent Applications available in IFICDB, IFIPAT, and IFIUDB Apr 19 NEWS Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS NEWS Apr 22 BIOSIS Gene Names now available in TOXCENTER NEWS Apr 22 Federal Research in Progress (FEDRIP) now available NEWS Apr 22 New e-mail delivery for search results now available Jun 03 NEWS Jun 10 MEDLINE Reload NEWS 10 Jun 10 PCTFULL has been reloaded NEWS 11 FOREGE no longer contains STANDARDS file segment Jul 02 NEWS 12 USAN to be reloaded July 28, 2002; NEWS 13 Jul 22 saved answer sets no longer valid Enhanced polymer searching in REGISTRY Jul 29 NEWS 14 Jul 30 NETFIRST to be removed from STN NEWS 15 Aug 08 CANCERLIT reload NEWS 16 PHARMAMarketLetter(PHARMAML) - new on STN NEWS 17 Aug 08 NTIS has been reloaded and enhanced NEWS 18 Aug 08 Aquatic Toxicity Information Retrieval (AQUIRE) NEWS 19 Aug 19 now available on STN IFIPAT, IFICDB, and IFIUDB have been reloaded NEWS 20 Aug 19 The MEDLINE file segment of TOXCENTER has been reloaded NEWS 21 Aug 19 NEWS 22 Aug 26 Sequence searching in REGISTRY enhanced JAPIO has been reloaded and enhanced NEWS 23 Sep 03 Experimental properties added to the REGISTRY file Sep 16 NEWS 24 CA Section Thesaurus available in CAPLUS and CA NEWS 25 Sep 16 NEWS 26 Oct 01 CASREACT Enriched with Reactions from 1907 to 1985 NEWS 27 Oct 21 EVENTLINE has been reloaded NEWS 28 Oct 24 BEILSTEIN adds new search fields Nutraceuticals International (NUTRACEUT) now available on STN NEWS 29 Oct 24 MEDLINE SDI run of October 8, 2002 NEWS 30 Oct 25 NEWS 31 Nov 18 DKILIT has been renamed APOLLIT More calculated properties added to REGISTRY NEWS 32 Nov 25 NEWS 33 Dec 02 TIBKAT will be removed from STN CSA files on STN NEWS 34 Dec 04 PCTFULL now covers WP/PCT Applications from 1978 to date NEWS 35 Dec 17 TOXCENTER enhanced with additional content Dec 17 NEWS 36 Adis Clinical Trials Insight now available on STN Dec 17 NEWS 37 NEWS 38 Dec 30 ISMEC no longer available Indexing added to some pre-1967 records in CA/CAPLUS NEWS 39 Jan 13 January 6 CURRENT WINDOWS VERSION IS V6.01a, NEWS EXPRESS CURRENT MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP), AND CURRENT DISCOVER FILE IS DATED 01 OCTOBER 2002 STN Operating Hours Plus Help Desk Availability NEWS HOURS General Internet Information NEWS INTER Welcome Banner and News Items NEWS LOGIN

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FILE 'HOME' ENTERED AT 10:30:42 ON 15 JAN 2003

=> file medline, dgene, embase, scisearch, uspatful, wpids, jicst, fsta
COST IN U.S. DOLLARS
SINCE FILE TOTAL
ENTRY SESSION
FULL ESTIMATED COST
0.42
0.42

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FILE 'FSTA' ENTERED AT 10:31:56 ON 15 JAN 2003 COPYRIGHT (C) 2003 International Food Information Service

=> s bone morphogenic protein L1 2316 BONE MORPHOGENIC PROTEIN

=> s osteochondral graft L3 125 OSTEOCHONDRAL GRAFT

=> s 11 () 12 () 13 L4 0 L1 (W) L2 (W) L3

=> s l1 and l2 L5 76 L1 AND L2

=> s 15 and 13 L6 1 L5 AND L3 => d 16 ti abs ibib tot

ANSWER 1 OF 1 USPATFULL L6

Device for regeneration of articular cartilage and TI

other tissue

An implantable device for facilitating the healing of voids in bone, AB cartilage and soft tissue is disclosed. A preferred embodiment includes a cartilage region comprising a polyelectrolytic complex joined with a subchondral bone region. The cartilage region, of this embodiment, enhances the environment for chondrocytes to grow articular cartilage; while the subchondral bone region enhances the environment for cells which migrate into that region's macrostructure and which differentiate into osteoblasts. A hydrophobic barrier exists between said regions, of this embodiment. In one embodiment, the polyelectrolytic complex transforms to hydrogel, following the implant procedure.

ACCESSION NUMBER:

2002:55324 USPATFULL

TITLE:

Device for regeneration of articular

cartilage and other tissue

INVENTOR(S):

Brekke, John H., Duluth, MN, UNITED STATES Goldman, Scott M., Paoli, PA, UNITED STATES

NUMBER KIND DATE _____ US 2002032488 A1 20020314 US 2001-909027 A1 20010719

PATENT INFORMATION: APPLICATION INFO.:

(9)

RELATED APPLN. INFO.:

Continuation-in-part of Ser. No. US 1998-206604, filed on 7 Dec 1998, GRANTED, Pat. No. US 6264701 Division of Ser. No. US 1994-242557, filed on 13 May 1994, GRANTED,

Pat. No. US 5981825

DOCUMENT TYPE: FILE SEGMENT:

Utility APPLICATION

LEGAL REPRESENTATIVE:

Alan D. Kamrath, Kensey Nash Corporation, 55 E. Uwchlan

Avenue, Exton, PA, 19341

NUMBER OF CLAIMS:

EXEMPLARY CLAIM:

LINE COUNT:

1349

=> d his

L1

L3

(FILE 'HOME' ENTERED AT 10:30:42 ON 15 JAN 2003)

FILE 'MEDLINE, DGENE, EMBASE, SCISEARCH, USPATFULL, WPIDS, JICST-EPLUS, FSTA' ENTERED AT 10:31:56 ON 15 JAN 2003

2316 S BONE MORPHOGENIC PROTEIN

L2 26968 S ARTICULAR CARTILAGE

125 S OSTEOCHONDRAL GRAFT

L40 S L1 () L2 () L3

76 S L1 AND L2 L5

1 S L5 AND L3 L6

=> s 13 and 11

1 L3 AND L1

=> d 17 ti abs ibib tot

ANSWER 1 OF 1 USPATFULL

тT Device for regeneration of articular cartilage and other tissue

An implantable device for facilitating the healing of voids in bone, AB cartilage and soft tissue is disclosed. A preferred embodiment includes a cartilage region comprising a polyelectrolytic complex joined with a

subchondral bone region. The cartilage region, of this embodiment, enhances the environment for chondrocytes to grow articular cartilage; while the subchondral bone region enhances the environment for cells which migrate into that region's macrostructure and which differentiate into osteoblasts. A hydrophobic barrier exists between said regions, of this embodiment. In one embodiment, the polyelectrolytic complex transforms to hydrogel, following the implant procedure.

2002:55324 USPATFULL ACCESSION NUMBER:

Device for regeneration of articular cartilage and TITLE:

other tissue

Brekke, John H., Duluth, MN, UNITED STATES INVENTOR(S):

Goldman, Scott M., Paoli, PA, UNITED STATES

NUMBER KIND DATE ______

US 2002032488 A1 20020314 US 2001-909027 A1 20010719 (9) PATENT INFORMATION:

APPLICATION INFO.:

Continuation-in-part of Ser. No. US 1998-206604, filed RELATED APPLN. INFO.:

on 7 Dec 1998, GRANTED, Pat. No. US 6264701 Division of Ser. No. US 1994-242557, filed on 13 May 1994, GRANTED,

Pat. No. US 5981825

DOCUMENT TYPE: Utility APPLICATION FILE SEGMENT:

Alan D. Kamrath, Kensey Nash Corporation, 55 E. Uwchlan LEGAL REPRESENTATIVE:

Avenue, Exton, PA, 19341

NUMBER OF CLAIMS: 56 EXEMPLARY CLAIM: 1 1349 LINE COUNT:

=> d his

(FILE 'HOME' ENTERED AT 10:30:42 ON 15 JAN 2003)

FILE 'MEDLINE, DGENE, EMBASE, SCISEARCH, USPATFULL, WPIDS, JICST-EPLUS, FSTA' ENTERED AT 10:31:56 ON 15 JAN 2003

2316 S BONE MORPHOGENIC PROTEIN

L1 L226968 S ARTICULAR CARTILAGE

125 S OSTEOCHONDRAL GRAFT L3

0 S L1 () L2 () L3 L4

76 S L1 AND L2 L5

1 S L5 AND L3 L6

L7 1 S L3 AND L1

=> d 15 ti abs ibib 1-10

ANSWER 1 OF 76 MEDLINE

Long-term effect of nitric oxide synthase inhibitor on repair of TΤ articular cartilage defects repairing.

OBJECTIVE: To discuss the long-term effect of inducible nitric oxide AB synthase inhibitor S-methylisothiourea (SMT) on repair of articular cartilage defects. METHODS: Twenty-four adult New Zealand White rabbits with full-thickness defects of cartilage created in the trochlear groove of their bilateral femurs were divided into three groups randomly, 8 in each group: (1) control group in which nothing was filled into the defects; (2) BMP group in which the defects were filled with collagen fibrin gel impregnated with recombinant human bone morphogenic protein (rhBMP); and (3) SMT group in which the defects were filled with collagen fibrin gel impregnated with rhBMP and hypodermic injection of SMT (5 mg .(-1) 12 h(-1)) was given. The animals were killed one year later. The gross appearance of the defects was assessed. The amount of released NO and the activity of NOS were examined by chemical colorimetry. The distribution of collagen was

examined by immunohistochemistry. The proteoglycan synthesis and cell activity was assessed by incorporation of radiolabelled sodium sulphate Na(2)(35)SO(4) and bromodeoxyuridine. RESULTS: One year after the defects in SMT group showed greater improvement in margin integration, cellular morphology, and architecture within defect than those in BMP group and control group (P < 0.01). Immunohistochemistry showed that there was less type-I collagen and more type-II collagen in SMT group than in the other two groups. Radiolabelled sodium sulphate (Na(2)(35)SO(4)) incorporation test showed that the proteoglycan synthesis in defects was higher in SMT group than in the other two groups (P < 0.01). BrdU incorporation test showed cells in repaired tissue with remarkable proliferous activity. CONCLUSION: iNOS inhibitor SMT significantly improves the quality of repair of defected cartilage and delays its degradation.

ACCESSION NUMBER:

2002215446 MEDLINE

DOCUMENT NUMBER:

21951165 PubMed ID: 11953121

TITLE:

Long-term effect of nitric oxide synthase inhibitor on

repair of articular cartilage defects

repairing.

AUTHOR:

Sun Wei; Wang Jixing; Jin Dadi; Liu Xiaoxia

CORPORATE SOURCE:

Department of Orthopaedics Surgery, Nanfang Hospital

Affiliated to First Militery Medical University, Guangzhou

510515, China.

SOURCE:

CHUNG-HUA I HSUEH TSA CHIH [CHINESE MEDICAL JOURNAL], (2002

Jan 10) 82 (1) 23-6.

Journal code: 7511141. ISSN: 0376-2491.

PUB. COUNTRY:

China

DOCUMENT TYPE:

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE:

Chinese

FILE SEGMENT:

Priority Journals

ENTRY MONTH:

200205

ENTRY DATE:

Entered STN: 20020416

Last Updated on STN: 20020515 Entered Medline: 20020514

L5 ANSWER 2 OF 76 MEDLINE

TI Enhanced matrix synthesis and in vitro formation of cartilage-like tissue by genetically modified chondrocytes expressing BMP-7.

Bone morphogenic protein-7 (BMP-7) supports ectopic cartilage and bone formation, is expressed in normal articular cartilage, and increases matrix synthesis in chondrocytes. Based on this knowledge, we hypothesized that an adenovirus (Ad) vector encoding human BMP-7 could be used to modify chondrocytes genetically to improve their capacity for cartilage repair. An adenovirus vector encoding BMP-7 (AdBMP-7) was constructed and its bioactivity confirmed by ectopic bone formation assay. AdBMP-7 modification of bovine chondrocytes induced expression of BMP-7 mRNA and bioactive protein, resulting in an increase in incorporation of 35SO4- into proteoglycan, 3H-proline uptake into protein, and the expression of the cartilage-specific matrix genes, aggrecan and type II collagen. An in vitro model of chondrocyte transplantation was used to demonstrate the feasibility of using genetically modified chondrocytes to enhance formation of cartilage-like tissue. When transplanted onto cartilage explants and maintained in vitro for 3 weeks, chondrocytes modified with AdBMP-7 formed 1.9-fold thicker tissue than chondrocytes modified with a control vector (P < 0.001). This tissue was positive for type II collagen and proteoglycan but negative for type X collagen and demonstrated a cartilage-like morphology. These observations suggest that Ad-mediated transfer of BMP-7 gene to chondrocytes enhances the chondrocyte-specific matrix synthesis and their capacity to form cartilage-like tissue, thus representing a strategy that may improve cell-based cartilage repair.

ACCESSION NUMBER:

2001514436 MEDLINE

DOCUMENT NUMBER:

21446023 PubMed ID: 11562118

TITLE:

Enhanced matrix synthesis and in vitro formation of cartilage-like tissue by genetically modified chondrocytes

expressing BMP-7.

AUTHOR: Hidaka C; Quitoriano M; Warren R F; Crystal R G

CORPORATE SOURCE: Division of Pulmonary and Critical Care Medicine, Weill

Medical College of Cornell University, New York, NY, USA...

geneticmedicine@mail.med.cornell.edu

CONTRACT NUMBER: T32-AR07281 (NIAMS)

SOURCE: JOURNAL OF ORTHOPAEDIC RESEARCH, (2001 Sep) 19 (5) 751-8.

Journal code: 8404726. ISSN: 0736-0266.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200110

ENTRY DATE: Entered STN: 20010920

Last Updated on STN: 20011008 Entered Medline: 20011004

L5 ANSWER 3 OF 76 MEDLINE

TI Cartilage and bone regeneration using gene-enhanced tissue engineering.

AB Joint cartilage injury remains a major problem in orthopaedics with more than 500,000 cartilage repair procedures performed yearly in the United States at a cost of hundreds of millions of dollars. No consistently reliable means to regenerate joint cartilage currently exists. The technologies of gene therapy and tissue engineering were combined using a retroviral vector to stably introduce the human bone morphogenic protein-7 complementary deoxyribonucleic acid into periosteal-derived rabbit mesenchymal stem cells. Bone morphogenic protein-7 secreting gene modified cells

subsequently were expanded in monolayer culture, seeded onto polyglycolic acid grafts, implanted into a rabbit knee osteochondral defect model, and evaluated for bone and cartilage repair after 4, 8, and 12 weeks. The grafts containing bone morphogenic protein-7

gene modified cells consistently showed complete or near complete bone and articular cartilage regeneration at 8 and 12 weeks

whereas the grafts from the control groups had poor repair as judged by macroscopic, histologic, and immunohistologic criteria. This is the first report of articular cartilage regeneration using a

combined gene therapy and tissue engineering approach.

ACCESSION NUMBER: 2000488818 MEDLINE

DOCUMENT NUMBER: 20492911 PubMed ID: 11039767

TITLE: Cartilage and bone regeneration using gene-enhanced tissue

engineering.

AUTHOR: Mason J M; Breitbart A S; Barcia M; Porti D; Pergolizzi R

G; Grande D A

CORPORATE SOURCE: Department of Research, North Shore University Hospital-New

York University School of Medicine, Manhasset 11030, USA.

SOURCE: CLINICAL ORTHOPAEDICS AND RELATED RESEARCH, (2000 Oct) (379

Suppl) S171-8.

Journal code: 0075674. ISSN: 0009-921X.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals

ENTRY MONTH: 200011

ENTRY DATE: Entered STN: 20010322

Last Updated on STN: 20010322 Entered Medline: 20001103

L5 ANSWER 4 OF 76 DGENE (C) 2003 THOMSON DERWENT

Isolated DNA encoding human SDF-5 protein - useful for controlling growth, differentiation etc. of cells, particularly of chondrocytes for treatment of arthritis etc., also pancreatic cells

AN AAW49082 Protein DGENE

AB The sequence is that of human SDF-5, a member of the Frazzled protein

family. Cells transformed with a vector containing the sequence are used to regulate genes, particularly pancreatic genes, or in combination with bone morphogenic protein 2 (BMP2), to

increase differentiation of progenitor cells into chondrocytes. The protein may be used to treat osteoarthritis, rheumatoid arthritis, or articular cartilage defects, also to increase/inhibit

articular cartilage defects, also to increase/inhibit cell formation, growth, differentiation, proliferation and/or maintenance in many other organs or tissues, e.g. for prevention or treatment of pancreatic cancer, diabetes (by inducing de novo formation of islet cells), other tissue defects, also to improve healing of wounds and to increase survival of nervous system cells, e.g. in cases of transplants The coding sequence can be used in gene therapy, and its fragments to detect related mRNA, while the protein is also used to generate antibodies, useful for affinity purification and as immunoassay reagents. Many other potential uses/activities for the gene and its encoded are contemplated but not exemplified, e.g. as cytokines, immuno-suppressants or immunostimulants, regulators of haematopoiesis, as fertility-control agents, haemostatic or thrombolytic agents, anti-inflammatory agents, antimicrobials, modulators of biorhythms and many more.

ACCESSION NUMBER: AAW49082 Protein DGENE

TITLE: Isolated DNA encoding human SDF-5 protein - useful for

controlling growth, differentiation etc. of cells,

particularly of chondrocytes for treatment of arthritis etc.,

69p

also pancreatic cells

INVENTOR: Lavallie E R; Racie L A
PATENT ASSIGNEE: (GEMY)GENETICS INST INC.
PATENT INFO: WO 9835043 A1 19980813

APPLICATION INFO: WO 1997-US18369 19971015 PRIORITY INFO: US 1997-848439 19970508 US 1997-796153 19970206

DOCUMENT TYPE: Patent LANGUAGE: English

OTHER SOURCE: 1998-447240 [38]

L5 ANSWER 5 OF 76 DGENE (C) 2003 THOMSON DERWENT

TI Isolated DNA encoding human SDF-5 protein - useful for controlling growth, differentiation etc. of cells, particularly of chondrocytes for treatment of arthritis etc., also pancreatic cells

AN AAV32930 DNA DGENE

The sequence is that encoding human SDF-5, a member of the Frazzled AB protein family. Cells transformed with a vector containing the sequence are used to regulate genes, particularly pancreatic genes, or in combination with bone morphogenic protein 2 (BMP2), to increase differentiation of progenitor cells into chondrocytes. The protein may be used to treat osteoarthritis, rheumatoid arthritis, or articular cartilage defects, also to increase/inhibit cell formation, growth, differentiation, proliferation and/or maintenance in many other organs or tissues, e.g. for prevention or treatment of pancreatic cancer, diabetes (by inducing de novo formation of islet cells), other tissue defects, also to improve healing of wounds and to increase survival of nervous system cells, e.g. in cases of transplants The coding sequence can be used in gene therapy, and its fragments to detect related mRNA, while the protein is also used to generate antibodies, useful for affinity purification and as immunoassay reagents. Many other potential uses/activities for the gene and its encoded are contemplated but not exemplified, e.g. as cytokines, immuno-suppressants or immunostimulants, regulators of haematopoiesis, as fertility-control agents, haemostatic or thrombolytic agents, anti-inflammatory agents, antimicrobials, modulators of biorhythms and

ACCESSION NUMBER: AAV32930 DNA DGENE

many more.

TITLE: Isolated DNA encoding human SDF-5 protein - useful for controlling growth, differentiation etc. of cells,

particularly of chondrocytes for treatment of arthritis etc.,

also pancreatic cells

INVENTOR: Lavallie E R; Racie L A
PATENT ASSIGNEE: (GEMY)GENETICS INST INC.
PATENT INFO: WO 9835043 A1 19980813

APPLICATION INFO: WO 1997-US18369 19971015 PRIORITY INFO: US 1997-848439 19970508

US 1997-796153 19970206

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: 1998-447240 [38]

L5 ANSWER 6 OF 76 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

TI Enhanced matrix synthesis and in vitro formation of cartilage-like tissue by genetically modified chondrocytes expressing BMP-7.

AB Bone morphogenic protein-7 (BMP-7) supports

ectopic cartilage and bone formation, is expressed in normal articular cartilage, and increases matrix synthesis in chondrocytes. Based on this knowledge, we hypothesized that an adenovirus (Ad) vector encoding human BMP-7 could be used to modify chondrocytes genetically to improve their capacity for cartilage repair. An adenovirus vector encoding BMP-7 (AdBMP-7) was constructed and its bioactivity confirmed by ectopic bone formation assay. AdBMP-7 modification of bovine chondrocytes induced expression of BMP-7 mRNA and bioactive protein, resulting in an increase in incorporation of (35)SO(-)(4) into proteoglycan, (3) H-proline uptake into protein, and the expression of the cartilage-specific matrix genes, aggrecan and type II collagen. An in vitro model of chondrocyte transplantation was used to demonstrate the feasibility of using genetically modified chondrocytes to enhance formation of cartilage-like tissue. When transplanted onto cartilage explants and maintained in vitro for 3 weeks, chondrocytes modified with AdBMP-7 formed 1.9-fold thicker tissue than chondrocytes modified with a control vector (P < 0.001). This tissue was positive for type II collagen and proteoglycan but negative for type X collagen and demonstrated a cartilage-like morphology. These observations suggest that Ad-mediated transfer of BMP-7 gene to chondrocytes enhances the chondrocyte-specific matrix synthesis and their capacity to form cartilage-like tissue, thus representing a strategy that may improve cell-based cartilage repair. .COPYRGT. 2001. Orthopaedic Research Society. Published by Elsevier

Science Ltd. All rights reserved.

ACCESSION NUMBER: 2001305182 EMBASE

TITLE: Enhanced matrix synthesis and in vitro formation of

cartilage-like tissue by genetically modified chondrocytes

expressing BMP-7.

AUTHOR: Hidaka C.; Quitoriano M.; Warren R.F.; Crystal R.G.

CORPORATE SOURCE: C. Hidaka, Institute of Genetic Medicine, Weill Medical

Coll. of Cornell Univ., New York, NY 10021, United States.

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SOURCE: Journal of Orthopaedic Research, (2001) 19/5 (751-758).

Refs: 40

ISSN: 0736-0266 CODEN: JOREDR

PUBLISHER IDENT.: S 0736-0266(01)00019-5

COUNTRY:

DOCUMENT TYPE:

FILE SEGMENT:

United Kingdom
Journal; Article
004 Microbiology
022 Human Genetics

029 Clinical Biochemistry 033 Orthopedic Surgery

LANGUAGE: English SUMMARY LANGUAGE: English

L5 ANSWER 7 OF 76 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

TI Cartilage and bone regeneration using gene-enhanced tissue engineering.

AB Joint cartilage injury remains a major problem in orthopaedics with more than 500,000 cartilage repair procedures performed yearly in the United

ae6

States at a cost of hundreds of millions of dollars. No consistently reliable means to reqenerate joint cartilage currently exists. The technologies of gene therapy and tissue engineering were combined using a retroviral vector to stably introduce the human bone

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whereas the grafts from the control groups had poor repair as judged by macroscopic, histologic, and immunohistologic criteria. This is the first report of articular cartilage regeneration using a

combined gene therapy and tissue engineering approach.

ACCESSION NUMBER:

2000362559 EMBASE

Cartilage and bone regeneration using gene-enhanced tissue TITLE:

engineering.

Mason J.M.; Breitbart A.S.; Barcia M.; Porti D.; Pergolizzi AUTHOR:

R.G.; Grande D.A.

Dr. J.M. Mason, Gene Therapy Vector Laboratory, Department CORPORATE SOURCE:

of Research, North Shore University Hospital, 350 Community

Drive, Manhasset, NY 11030, United States

Clinical Orthopaedics and Related Research, (2000) -/379 SOURCE:

SUPPL. (S171-S178).

Refs: 27

ISSN: 0009-921X CODEN: CORTBR

United States COUNTRY:

Journal; Conference Article DOCUMENT TYPE:

Human Genetics FILE SEGMENT: 022

Orthopedic Surgery 033

036 Health Policy, Economics and Management

LANGUAGE: English SUMMARY LANGUAGE: English

ANSWER 8 OF 76 SCISEARCH COPYRIGHT 2003 ISI (R) L_5

Cartilage and bone regeneration using gene-enhanced tissue engineering ΤI Joint cartilage injury remains a major problem in orthopaedics with AΒ

more than 500,000 cartilage repair procedures performed yearly in the United States at a cost of hundreds of millions of dollars. No consistently reliable means to regenerate joint cartilage currently exists. The technologies of gene therapy and tissue engineering were combined using a retroviral vector to stably introduce the human hone morphogenic protein-7 complementary deoxyribonucleic acid into

periosteal-derived rabbit mesenchymal stem cells. Bone

morphogenic protein-7 secreting gene modified cells

subsequently were expanded in monolayer culture, seeded onto polyglycolic acid grafts, implanted into a rabbit knee osteochondral defect model, and evaluated for bone and cartilage repair after 4, 8, and 12 weeks, The grafts containing bone morphogenic protein-7

gene modified cells consistently showed complete or near complete bone and articular cartilage regeneration at 8 and 12 weeks

whereas the grafts from the control groups had poor repair as judged by macroscopic, histologic, and immunohistologic criteria, This is the first report of articular cartilage regeneration using a combined gene therapy and tissue engineering approach.

2000:777821 SCISEARCH

ACCESSION NUMBER: THE GENUINE ARTICLE: 362NP

TITLE: Cartilage and bone regeneration using gene-enhanced tissue

engineering

Mason J M (Reprint); Breitbart A S; Barcia M; Porti D; AUTHOR:

Pergolizzi R G; Grande D A

NYU, GENE THERAPY VECTOR LAB, DEPT RES, N SHORE UNIV HOSP, CORPORATE SOURCE:

> SCH MED, 350 COMMUNITY DR, MANHASSET, NY 11030 (Reprint); NYU, DIV PLAST & RECONSTRUCT SURG, SCH MED, N SHORE UNIV HOSP, MANHASSET, NY 11030; NYU, DIV ORTHOPED SURG, SCH MED, N SHORE UNIV HOSP, DEPT SURG, MANHASSET, NY 11030

COUNTRY OF AUTHOR:

USA

SOURCE:

CLINICAL ORTHOPAEDICS AND RELATED RESEARCH, (OCT 2000) No.

379, Supp. [S], pp. S171-S178.

Publisher: LIPPINCOTT WILLIAMS & WILKINS, 530 WALNUT ST,

PHILADELPHIA, PA 19106-3621.

ISSN: 0009-921X.

DOCUMENT TYPE: FILE SEGMENT:

Article; Journal

LIFE; CLIN

LANGUAGE:

English

REFERENCE COUNT:

27 *ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

L5 ANSWER 9 OF 76 USPATFULL

Secreted and transmembrane polypeptides and nucleic acids encoding the ΤI

The present invention is directed to novel polypeptides and to nucleic AΒ acid molecules encoding those polypeptides. Also provided herein are vectors and host cells comprising those nucleic acid sequences, chimeric polypeptide molecules comprising the polypeptides of the present invention fused to heterologous polypeptide sequences, antibodies which bind to the polypeptides of the present invention and to methods for producing the polypeptides of the present invention.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:

2003:3495 USPATFULL

TITLE:

Secreted and transmembrane polypeptides and nucleic

acids encoding the same

INVENTOR(S):

Ashkenazi, Avi, San Mateo, CA, UNITED STATES Botstein, David, Belmont, CA, UNITED STATES Desnoyers, Luc, San Francisco, CA, UNITED STATES Eaton, Dan L., San Rafael, CA, UNITED STATES

Ferrara, Napoleone, San Francisco, CA, UNITED STATES Filvaroff, Ellen, San Francisco, CA, UNITED STATES

Fong, Sherman, Alameda, CA, UNITED STATES Gao, Wei-Qiang, Palo Alto, CA, UNITED STATES

Gerber, Hanspeter, San Francisco, CA, UNITED STATES Gerritsen, Mary E., San Mateo, CA, UNITED STATES Goddard, Audrey, San Francisco, CA, UNITED STATES Godowski, Paul J., Burlingame, CA, UNITED STATES Grimaldi, J. Christopher, San Francisco, CA, UNITED

STATES

Gurney, Austin L., Belmont, CA, UNITED STATES

Hillan, Kenneth J., San Francisco, CA, UNITED STATES Kljavin, Ivar J., Lafayette, CA, UNITED STATES Mather, Jennie P., Millbrae, CA, UNITED STATES

Pan, James, Belmont, CA, UNITED STATES

Paoni, Nicholas F., Belmont, CA, UNITED STATES Roy, Margaret Ann, San Francisco, CA, UNITED STATES Stewart, Timothy A., San Francisco, CA, UNITED STATES

Tumas, Daniel, Orinda, CA, UNITED STATES

Williams, P. Mickey, Half Moon Bay, CA, UNITED STATES Wood, William I., Hillsborough, CA, UNITED STATES

(9)

PATENT ASSIGNEE(S): Genentech, Inc. (U.S. corporation)

> KIND NUMBER DATE

PATENT INFORMATION: US 2003003530 A1 20030102 US 2001-904011 A1 20010711 APPLICATION INFO.:

RELATED APPLN. INFO.: Continuation of Ser. No. US 2000-665350, filed on 18

NUMBER

DATE

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	NUMBER	DATE	
	1000 11010024	19980910	
	1998-US18824		
WO	1998-US19177	19980914	
WO	1998-US19330	19980916	
WO	1998-US19437	19980917	
WO	1998-US25108	19981201	
WO	1999-US20594	19990908	
WO	1999-US20944	19990913	
WO	1999-US21090	19990915	
WO	1999-US21547	19990915	
WO	1999-US23089	19991005	
WO	1999-US28214	19991129	
WO	1999-US28313	19991130	
WO	1999-US28301	19991201	
WO	1999-US28564	19991202	
WO	1999-US28565	19991202	
WO	1999-US30095	19991216	
WO	1999-US30999	19991220	
WO	1999-US30911	19991220	
WO	2000-US219	20000105	
WO	2000-US3565	20000211	
WO	2000-US4414	20000222	
WO	2000-US5004	20000224	
WO	2000-US5841	20000302	
WO	2000-US7377	20000320	
WO	2000-US8439	20000330	
WO	2000-US14042	20000522	
WO	2000-US15264	20000602	
WO	2000-US20710	20000728	
WO	2000-US23328	20000824	
US	1997-59115P	19970917	(60)
US	1997-59184P	19970917	(60)
US	1997-59122P	19970917	(60)
US	1997-59117P	19970917	(60)
US	1997-59113P	19970917	(60)
US	1997-59121P	19970917	(60)
US	1997-59119P	19970917	(60)
US	1997-59263P	19970918	
US	1997-59266P	19970918	(60)
US	1997-62125P	19971015	(60)
US	1997-62287P	19971017	
US	1997-62285P	19971017	
US	1997-63486P	19971021	(60)
US	1997-62816P	19971024	(60)
US	1997-62814P	19971024	(60)
US	1997-63127P	19971024	(60)
US	1997-63120P	19971024	(60)
US	1997-63121P	19971024	(60)
US	1997-63045P	19971024	(60)
US	1997-63128P	19971024	(60)
US	1997-63329P	19971027	(60)
US	1997-63327P	19971027	(60)
US	1997-63549P	19971028	(60)
US	1997-63541P	19971028	(60)
US	1997-63550P	19971028	(60)
US	1997-63542P	19971028	(60)
US	1997-63544P	19971028	(60)
US	1997-63564P	19971028	(60)
US	1997-63734P	19971029	(60)
US	1997-63738P	19971029	(60)
US	1997-63704P	19971029	(60)

19971029 (60) US 1997-63435P US 1997-64215P 19971029 (60) US 1997-63735P 19971029 (60) US 1997-63732P 19971029 (60) US 1997-64103P 19971031 (60) US 1997-63870P 19971031 (60) US 1997-64248P 19971103 (60) US 1997-64809P 19971107 (60) US 1997-65186P 19971112 (60) US 1997-65846P 19971117 (60) 19971118 (60) US 1997-65693P 19971121 (60) US 1997-66120P 19971121 (60) US 1997-66364P 19971124 (60) US 1997-66772P 19971124 (60) US 1997-66466P 19971124 (60) US 1997-66770P 19971124 (60) US 1997-66511P US 1997-66453P 19971124 (60)

DOCUMENT TYPE: FILE SEGMENT:

Utility APPLICATION

LEGAL REPRESENTATIVE:

BRINKS HOFER GILSON & LIONE, P.O. BOX 10395, CHICAGO,

IL, 60610

NUMBER OF CLAIMS: EXEMPLARY CLAIM:

38

NUMBER OF DRAWINGS:

124 Drawing Page(s)

LINE COUNT:

21255

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

1.5 ANSWER 10 OF 76 USPATFULL

Secreted and transmembrane polypeptides and nucleic acids encoding the ΤI

The present invention is directed to novel polypeptides and to nucleic AB acid molecules encoding those polypeptides. Also provided herein are vectors and host cells comprising those nucleic acid sequences, chimeric polypeptide molecules comprising the polypeptides of the present invention fused to heterologous polypeptide sequences, antibodies which bind to the polypeptides of the present invention and to methods for producing the polypeptides of the present invention.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:

2002:344632 USPATFULL

TITLE:

Secreted and transmembrane polypeptides and nucleic

acids encoding the same

INVENTOR (S):

Ashkenazi, Avi, San Mateo, CA, UNITED STATES Botstein, David, Belmont, CA, UNITED STATES Desnoyers, Luc, San Francisco, CA, UNITED STATES Eaton, Dan L., San Rafael, CA, UNITED STATES Ferrara, Napoleone, San Francisco, CA, UNITED STATES Filvaroff, Ellen, San Francisco, CA, UNITED STATES Fong, Sherman, Alameda, CA, UNITED STATES Gao, Wei-Qiang, Palo Alto, CA, UNITED STATES Gerber, Hanspeter, San Francisco, CA, UNITED STATES Gerritsen, Mary E., San Mateo, CA, UNITED STATES

Goddard, Audrey, San Francisco, CA, UNITED STATES Godowski, Paul J., Burlingame, CA, UNITED STATES Grimaldi, J. Christopher, San Francisco, CA, UNITED **STATES**

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Paoni, Nicholas F., Belmont, CA, UNITED STATES Roy, Margaret Ann, San Francisco, CA, UNITED STATES Stewart, Timothy A., San Francisco, CA, UNITED STATES Tumas, Daniel, Orinda, CA, UNITED STATES Williams, P. Mickey, Half Moon Bay, CA, UNITED STATES

Wood, William I., Hillsborough, CA, UNITED STATES

Genentech, Inc. (U.S. corporation) PATENT ASSIGNEE(S):

> KIND DATE NUMBER _____ US 2002198366 A1 20021226 US 2001-907841 A1 20010717 (9)

PATENT INFORMATION: APPLICATION INFO.: RELATED APPLN. INFO.:

Continuation of Ser. No. US 2000-665350, filed on 18

Sep 2000, PENDING

PRIORITY INFORMATION:

WO 1998-US18824 19980910 WO 1998-US19177 19980914 WO 1998-US19330 19980916 WO 1998-US19437 19980917 WO 1998-US25108 19981201 WO 1999-US20594 19990908 WO 1999-US21090 19990915 WO 1999-US21547 19990915 WO 1999-US23089 19991005 WO 1999-US28313 19991130 WO 1999-US28313 19991130 WO 1999-US28564 19991202 WO 1999-US28564 19991202 WO 1999-US28565 19991202 WO 1999-US30095 19991216 WO 1999-US30095 19991216 WO 1999-US30095 19991220 WO 1999-US30095 19991220 WO 2000-US3565 20000211 WO 2000-US3565 20000211 WO 2000-US5004 20000224 WO 2000-US5004 20000224 WO 2000-US5004 20000224 WO 2000-US504 20000330 WO 2000-US14042 20000522 WO 2000-US15264 20000602 WO 2000-US14042 2000728 WO 2000-US15264 20000602 WO 2000-US23328 20000824 US 1997-59115P 19970917 (60) US 1997-5912P 19970917 (60) US 1997-5912P 19970917 (60) US 1997-5912P 19970917 (60) US 1997-62125P 19970917 (60) US 1997-62125P 19970918 (60) US 1997-6286P 19971015 (60) US 1997-6286P 19971014 (60) US 1997-63121P 19971024 (60) US 1997-63128P 19971024 (60) US 1997-63128P 19971024 (60)	NUMBER	DATE	
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WEST

Generate Collection

L2: Entry 3 of 5

File: USPT

Feb 3, 1998

DOCUMENT-IDENTIFIER: US 5713374 A TITLE: Fixation method for the attachment of wound repair materials to cartilage defects

BSPR:

Techniques were developed to utilize autologous tissue, such as transplantation of: 1) osteochondral grafts (DePalma, et al. 1963); 2) chondrocytes (Grande, et al. 1989); 3) periosteum (Homminga, et al., 1990); and 4) demineralized bone (Dahlberg and Kreicbers, 1991). These techniques have been used to transplant whole or partial joints, with mixed results. For example, a number of investigators attempted to heal cartilage defects using chondrocytes isolated from epiphysial plates, as well as articular cells, with the hypothesis that these cells would have a greater chance of success due to their heightened metabolism (Itay, et al. 1987). Clinical studies using cultured cells reported excellent results, showing a significant decrease in pain and restoration of normal function after two to four years post-op (Iloika, et al. 1990; Ilomminga, et al. 1990).

End of Result Set

Generate Collection

L2: Entry 5 of 5

File: USPT

Feb 10, 1987

DOCUMENT-IDENTIFIER: US 4642120 A TITLE: Repair of cartilage and bones

BSPR:

When articular cartilage is damaged by trauma, infection or degenerative processes, such damages generally fail to heal or even improve. Hitherto various attempts have been made to resort to osteochondral grafts and to the provision of various forms of prosthesis, but long term results have been poor and discouraging. There have been reported attempts to use cultured chondrocytes as a source of cartilage transplants, but integration of the transplants with the neighboring cartilage was generally unsatisfactory.

5226914

Page 1

DUPLICATE 4

L16 ANSWER 7 OF 8 MEDLINE

97270218

MEDLINE

ACCESSION NUMBER: DOCUMENT NUMBER:

97270218

TITLE:

Regeneration of articular

cartilage defects in rabbits by osteogenic

protein-1 (bone morphogenetic

protein-7).

AUTHOR:

Grgic M; Jelic M; Basic V; Basic N; Pecina M; Vukicevic S Drago Perovic Institute of Anatomy, School of Medicine,

University of Zagreb, Croatia.

SOURCE:

ACTA MEDICA CROATICA, (1997) 51 (1) 23-7.

Journal code: BH2. ISSN: 1330-0164.

PUB. COUNTRY:

Croatia

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE:

English 199707

ENTRY MONTH:

CORPORATE SOURCE:

Osteogenic protein-1 (OP-1, BMP-7), a member of the transforming growth factor-beta family, induces cartilage and bone formation when implanted at intra and extraskeletal sites in vivo. The human OP-1 gene has been cloned and biologically active recombinant OP-1 homodimers have been produced. In the present study, the authors investigated the influence of OP-1 on healing of full-thickness articular cartilage defects, made by drilling two adjacent (phi 3mm) holes through articular cartilage of NZW rabbit knee joint were dissected and examined histomorphometrically. Results indicated that OP-1 induced articular cartilage healing and

regeneration of the joint surface which contained cells resembling mature joint chondrocytes. These data imply a new strategy for biological repair of damaged joint surfaces in humans.

L17 ANSWER 2 OF 4 MEDLINE

ACCESSION NUMBER:

93101749 MEDLINE

DOCUMENT NUMBER:

93101749

TITLE:

Reconstruction of the bone--bone marrow organ by osteogenin, a bone morphogenetic protein, and

demineralized

bone matrix in calvarial defects of adult primates.

AUTHOR:

Ripamonti U; Ma S S; Cunningham N S; Yeates L; Reddi A H Medical Research Council/University of the Witwatersrand,

CORPORATE SOURCE:

Johannesburg, South Africa.

SOURCE:

PLASTIC AND RECONSTRUCTIVE SURGERY, (1993 Jan) 91 (1)

27-36.

Journal code: P9S. ISSN: 0032-1052.

PUB. COUNTRY:

United States

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE:

English

FILE SEGMENT:

Abridged Index Medicus Journals; Priority Journals

199303

ENTRY MONTH: Information concerning the efficacy of osteogenin, a bone morphogenetic protein, and demineralized bone matrix in

orthotopic sites in nonhuman primates is a prerequisite for potential clinical application in humans. After exposure of the calvaria, 84

cranial

defects, 25 mm in diameter, were prepared in 26 adult male baboons (Papio ursinus). Defects were implanted with insoluble collagenous bone matrix (ICBM, the inactive collagenous residue after dissociative extraction of bone matrix with 4 M guanidine hydrochloride) reconstituted with osteogenin fractions isolated from baboon bone matrix by chromatography

on

heparin-Sepharose and hydroxyapatite-Ultrogel (Og Hep-HA) or osteogenin further purified using Sephacryl S-200 gel filtration chromatography (Og S-200). Baboon osteogenin with the highest biologic activity in a rodent bioassay, as determined by alkaline phosphatase activity, calcium

content,

and histologic analysis, was used for orthotopic implantation in baboons. Additional defects were implanted with baboon demineralized bone matrix (DBM) or ICBM without osteogenin as control. Defects also were grafted with corticocancellous bone harvested from the iliac crest or left ungrafted to monitor the spontaneous regeneration potential of the adult baboon calvaria. Undecalcified bone sections at 7 microns were prepared from the harvested specimens 30 and 90 days after surgery. Histomorphometry demonstrated that Og S-200 induced copious amounts of bone and osteoid as early as day 30 (P < 0.01 versus ICBM, autogenous grafts and untreated defects). At day 90, in implants of Og S-200, Og Hep-HA, and DBM, bone and marrow formation was extensive, culminating in complete regeneration of the craniotomies. In implants of DBM, bone formed with an intervening phase of cartilage development. This provides the phenotypic evidence of endochondral bone differentiation by induction in defects of membranous calvarial bone in adult primates. These results establish the potential therapeutic application of osteogenin and demineralized bone matrix for the architectural reconstruction of the bone-bone marrow organ in humans.

Page 1

L17 ANSWER 4 OF 4 MEDLINE

ACCESSION NUMBER:

86278360

DOCUMENT NUMBER:

86278360

TITLE:

Bone repair induced by bone morphogenetic protein in ulnar

God I

defects in dogs.

AUTHOR:

Nilsson O S; Urist M R; Dawson E G; Schmalzried T P;

Finerman G A

SOURCE:

JOURNAL OF BONE AND JOINT SURGERY. BRITISH VOLUME, (1986

Aug) 68 (4) 635-42.

Journal code: HK7. ISSN: 0301-620X.

PUB. COUNTRY:

ENGLAND: United Kingdom

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE:

English

FILE SEGMENT:

Abridged Index Medicus Journals; Priority Journals

ENTRY MONTH: 198611

In dogs, resection of a length of the ulna equal to twice the diameter of the mid-shaft leaves a defect which consistently fails to unite. In

response to an implant of 100 mg of bovine bone

morphogenetic protein (BMP), the defect

becomes filled by callus consisting of fibrocartilage, cartilage and woven bone within four weeks. The cartilage is resorbed and replaced by new bone in four to eight weeks. Woven bone is then resorbed,

colonised by bone marrow cells and remodelled into lamellar bone. Union

of

the defect is produced by 12 weeks. Control defects filled with autogeneic

cortical bone chips unite after the same period. In regeneration induced by bone morphogenetic protein (

BMP) and in repair enhanced by bone graft, union depends upon the proliferation of cells within and around the bone ends. Our working hypothesis is that BMP induces the differentiation of perivascular connective tissue cells into chondroblasts and osteoprogenitor cells and thereby augments the process of bone regeneration from the cells already present in the endosteum and periosteum.

1/27

L17 ANSWER 1 OF 4 MEDLINE

DUPLICATE 1

ACCESSION NUMBER: DOCUMENT NUMBER:

96023917 96023917

TITLE:

Commercially-prepared allograft material has biological

activity in vitro.

AUTHOR:

Shigeyama Y; D'Errico J A; Stone R; Somerman M J Department of Periodontics/Prevention/Geriatrics,

University of Michigan, Ann Arbor, USA.

CONTRACT NUMBER:

CORPORATE SOURCE:

DE09532 (NIDCR)

SOURCE:

JOURNAL OF PERIODONTOLOGY, (1995 Jun) 66 (6) 478-87.

Journal code: JMT. ISSN: 0022-3492.

MEDLINE

PUB. COUNTRY:

United States

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE:

English

FILE SEGMENT:

Priority Journals; Dental Journals

ENTRY MONTH: 199601

The well-established finding that implantation of demineralized bone matrix at non-skeletal sites results in formation of cartilage and bone has been attributed to bone morphogenetic proteins/factors. Commercially-available demineralized bone allograft materials are being used currently to reconstruct/regenerate bone. The studies described here focused on establishing biological activity of protein extracts prepared from commercially obtained bone graft material in vitro. Furthermore, the biological activity of these protein extracts in vitro was compared with similar extracts prepared from freshly obtained

human bone. Biological activities of bone matrix proteins examined included their ability to promote proliferation, attachment, and migration

of gingival fibroblasts using an in vitro system. Guanidine followed by guanidine/EDTA was used to separate bone matrix proteins into proteins associated with soft tissues of bone and proteins retained within the mineral compartment, respectively. Two preparations of each starting material were tested and the biological activity of each preparation was evaluated in triplicate at least three times. Slot blot analysis revealed that commercially-prepared material contained type I collagen; fibronectin; BSP; and BMP-2, 4, and 7. However, the freshly prepared bone extracts appeared to have higher BMP concentrations. The ability of commercial extracts to promote cell proliferation, while significant, was limited and significantly less when compared with similar extracts prepared from freshly obtained bone. All extracts promoted cell attachment significantly, while none of the extracts promoted cell migration. Thus, commercially-prepared material retained proteins having the capacity to influence cell behavior in vivo. However, some biological activity as measured in vitro was lost as a result of tissue processing.

Page 1

L16 ANSWER 5 OF 8 MEDLINE
ACCESSION NUMBER: 1998258985 MEDLINE

DUPLICATE 2

DOCUMENT NUMBER:

98258985

TITLE:

Osteogenic protein (OP-1, BMP-7) stimulates cartilage differentiation of human and goat perichondrium tissue in

witro

AUTHOR:

Klein-Nulend J; Louwerse R T; Heyligers I C; Wuisman P I;

Semeins C M; Goei S W; Burger E H

CORPORATE SOURCE:

ACTA-Vrije Universiteit, Department of Oral Cell Biology,

Amsterdam, The Netherlands..

J.Klein_Nulend.OCB.ACTA@med.vu

.nl

SOURCE:

JOURNAL OF BIOMEDICAL MATERIALS RESEARCH, (1998 Jun 15) 40

(4) 614-20.

Journal code: HJJ. ISSN: 0021-9304.

PUB. COUNTRY:

United States

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE:

English

FILE SEGMENT:

Priority Journals

ENTRY MONTH:

199811

ENTRY WEEK:

19981104

AB The objective of this study was to examine in vitro the influence of recombinant human osteogenic protein-1 [rhOP-1, or bone

morphogenetic protein-7 (BMP-7)] on cartilage

formation by human and goat perichondrium tissue containing progenitor cells with chondrogenic potential. Fragments of outer ear perichondrium tissue were embedded in clotting autologous blood to which rhOP-1 had

been

added or not added (controls), and the resulting explant was cultured for 3 weeks without further addition of rhOP-1. Cartilage formation was monitored biochemically by measuring [35S]-sulphate incorporation into proteoglycans and histologically by monitoring the presence of metachromatic matrix with cells in nests. The presence of rhOP-1 in the explant at the beginning of culture stimulated [35S]-sulphate incorporation into proteoglycans in a dose-dependent manner after 3 weeks of culture. Maximal stimulation was reached at 40 microg/mL (human explants: +148%; goat explants: +116%). Histology revealed that explants treated with 20-200 microg/mL of rhOP-1, but not untreated control explants, contained areas of metachromatic-staining matrix with chondrocytes in cell nests. It was concluded that rhOP-1 stimulates differentiation of cartilage from perichondrium tissue. The direct

actions

of rhOP-1 on perichondrium cells in the stimulation of chondrocytic differentiation and production of cartilage matrix in vitro provides a cellular mechanism for the induction of cartilage formation by rhOP-1 in vivo. Thus rhOP-1 may promote early steps in the cascade of events leading

to cartilage formation and could prove to be an interesting factor in the regeneration of cartilage in articular cartilage defects.

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